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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,238	01/19/2006	Pnina Fishman	FISHMAN19B	9164

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EXAMINER	
SINGH, SATYENDRA K	
ART UNIT	PAPER NUMBER
1657	

MAIL DATE	DELIVERY MODE
09/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/565,238	FISHMAN ET AL.	
	Examiner	Art Unit	
	SATYENDRA K. SINGH	1657	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 September 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *NONE*.
   Claim(s) objected to: *NONE*.
   Claim(s) rejected: *15, 16, 18-21*.
   Claim(s) withdrawn from consideration: *22,23 and 25-28*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657

Continuation of 11. does NOT place the application in condition for allowance because: applicant's arguments as they pertain to the pending claims 15, 16 and 18-21 (as currently amended) have been fully considered but are not found to be persuasive for the following reasons of record:

First, applicant's arguments (see remarks, pages 7 and 8, in particular) regarding the restriction/lack of unity between the distinct process inventions of groups III and IV (as discussed in the previous rejection of record) is duly noted and fully considered. However, as stated earlier in the office action, the special technical feature of the pending claims requires the use of A3AR receptor agonist (i.e. subject suitable for anti-inflammatory therapeutic treatment by means of an A3 adenosine receptor agonist such as IB-MECA; see instant claims 15 and 22) in the diagnosis and/or treatment of inflammatory states, which has been disclosed and/or suggested in the cited prior art (such as collagen-induced arthritis in rats, an animal model for autoimmune diseases such as arthritis; Szabo et al, 1998; see restriction action, page 3; paper dated 5/16/08), the pending claims lack unity of invention. The argument that "Essentially, the same thing is being stated in two different ways. Additionally, the examiner cannot establish that there is a different field of search and that there would be a burden in searching both sets of claims" (see remarks, page 8) is fully considered. However it is not found to be persuasive because the invention of group II as recited in claim 22, requires the distinct method step of "determining that there is a greater probability that the subject will respond to said anti-inflammatory therapeutic treatment if said level is above a predefined threshold that is above the level of A3AR expression in WBCs of a healthy subject". Moreover, the argument of search burden (see also remarks, page 9) is not pertinent as per the requirement of PCT, if the separate inventions as currently claimed are found to lack unity of invention.

Regarding the obviousness rejection of record of pending claims 15, 16 and 18-21 over the cited prior art combination (Gessi et al taken with Rhodes & Campbell, and in view of Montesinos et al and Fishman & Bar-Yehuda), applicants argument (see remarks, pages 10-13) that "...the method of selecting an autoimmune disease patient that is most suitable for treatment with an A3AR agonist is nowhere taught or suggested by any of the references of record, either alone or in combination. Accordingly, reconsideration and withdrawal of this rejection are respectfully urged" is fully considered. However, it is not found to be persuasive because Gessi et al clearly disclose the diagnostic use of elevated levels of A3AR in peripheral blood cells (including white blood cells such as lymphocytes and neutrophils, measured using a receptor binding assay) of patients with an inflammatory state (albeit as a result of the colorectal cancer). The cited reference of Fishman & Bar-Yehuda clearly suggest the therapeutic applications of A3 receptor subtype, especially the use of agonists such as IB-MECA as one of the most potent therapeutic agents for the treatment of inflammation, which is believed to be mediated upon A3AR activation in neutrophils, eosinophils and macrophages (i.e. white blood cell components) via direct effect on the production of anti- inflammatory cytokines (see page 464, right column, in particular)7. Therefore, suggesting the use of agonist IB-MECA for activation of A3AR receptor to produce desired anti-inflammatory effects in subjects in need thereof, including its use in clinical settings. Montesinos et al, on the other hand, disclose the role of A3AR receptors, the activation of which is required for the inhibition of inflammation (i.e. for anti-inflammatory therapeutic treatment) by methotrexate commonly used for the therapy of chronic inflammatory diseases, including autoimmune joint disorders such as Rheumatoid Arthritis, thus clearly providing the nexus for the diagnostic use of A3AR receptor levels in white blood cells in patients (that can be suitably treated with the A3AR aginst IB-MECA) having inflammatory state as a result of autiimmune disease, such as Rheumatoid Arthritis.
The argument (see remarks, page 12, in particular) that "While Fishman and Montesinos relate to the use of an A3AR agonist in the treatment of autoimmune diseases, there is no suggestion therein that the level of A3AR expression in white blood cells of autoimmune patients may be used as a diagnostic for the presence of autoimmune disease, as Gessi does with respect to colon carcinoma" is noted and fully considered. However, it is not found to be persuasive because the combined teachings of the cited references of record clearly suggest a link between inflammation in patients (as a result of inflammatory states such as colorectal cancer and autoimmune diseases such as rheumatoid arthritis), the levels of A3AR receptor in peripheral blood cells such as white blood cells, and the use of A3AR agonist such as IB-MECA as an antiinflammatory drug in clinical settings, and therefore, the diagnostic process as currently claimed (see claim 15, in particular) would have been obvious to an artisan of ordinary skill in the clinical art, at the time the claimed invention was made. The obviousness rejection of record is therefore properly made and maintained.

/Satyendra K. Singh/
Examiner, AU 1657